We Claim:

1. A modified cytoplasmic dynein heavy chain1 polypeptide, wherein:

(a) the amino acid sequence of said modified cytoplasmic dynein heavy chain1 differs from the corresponding wild type sequence by substitution, deletion, or insertion of at least one amino acid in the wild type cytoplasmic dynein heavy chain1 sequence;

(b) a biological activity of said modified cytoplasmic dynein heavy chain1 polypeptide is altered by at least 10% in comparison to the activity of the wild type cytoplasmic dynein heavy chain1 polypeptide.

2. The modified cytoplasmic dynein heavy chain1 polypeptide of claim 1 wherein said biological activity is altered by at least 50% in comparison to the activity of the wild type cytoplasmic dynein heavy chain1 polypeptide.

3. The modified cytoplasmic dynein heavy chain1 polypeptide of claim 1 wherein said biological activity is altered by at least 75% in comparison to the activity of the wild type cytoplasmic dynein heavy chain1 polypeptide.

4. The modified cytoplasmic dynein heavy chain1 polypeptide of any of claims 1 to 3, wherein the alteration of said biological activity is a reduction of activity.

5. The modified cytoplasmic dynein heavy chain1 polypeptide of any of claims 1 to 3, wherein the alteration of said biological activity is an increase of activity.

6. The modified cytoplasmic dynein heavy chain1 polypeptide of any of claims 1 to 5, wherein the alteration of said biological activity is demonstrated by a method selected from the group consisting of:

(a) determining the relative proportions of cytoplasmic dynein heavy chain1 dimer and cytoplasmic dynein heavy chain1 monomer in a test sample;

(b) quantifying the proportion of cytoplasmic dynein complex that is fully assembled from its subunits in an *in vitro* assembly assay;

(c) quantifying the proportion of cytoplasmic dynein complex subunits that remain unassembled in an *in vitro* assembly assay;

(d) quantifying the proportion of cytoplasmic dynein heavy chain1 that binds to microtubules *in vitro*;

(e) assaying the rate of dimerization of the cytoplasmic dynein heavy chain1 polypeptide *in vitro*;

(f) assaying the rate of assembly of the cytoplasmic dynein complex from constituent subunits *in vitro*;

(g) assaying the rate of binding of cytoplasmic dynein heavy chain1 to microtubules *in vitro*;

(h) assaying motor activity of the cytoplasmic dynein complex *in vitro*;

(i) assaying motor activity of the cytoplasmic dynein heavy chain1 *in vitro*;

(j) quantifying binding of cytoplasmic dynein heavy chain1 polypeptide to an antibody having an epitope specific for cytoplasmic dynein heavy chain1; and

wherein the method compares the results provided by said modified cytoplasmic dynein heavy chain1 polypeptide to those provided by the corresponding wild type cytoplasmic dynein heavy chain1 polypeptide.

7. The modified cytoplasmic dynein heavy chain1 polypeptide of claim 6, wherein said antibody is selected from the following group;

(a) an antibody binding an epitope situated within the dimerization domain of the cytoplasmic dynein heavy chain1;

(b) an antibody binding an epitope situated within a binding domain of the cytoplasmic dynein heavy chain1 the binds a subunit of the cytoplasmic dynein complex;

(c) an antibody binding an epitope located in exon 12 of cytoplasmic dynein heavy chain1;

(d) an antibody binding an epitope located in exon 13 of cytoplasmic dynein heavy chain1;

(e) an antibody binding an epitope located in exons 12 plus 13 of cytoplasmic dynein heavy chain1;

(f) an antibody binding an epitope formed by the intact dimer of cytoplasmic dynein heavy chain1, but not by the individual monomers.

8. The modified cytoplasmic dynein heavy chain1 polypeptide of claim 6, wherein motor activity of the cytoplasmic dynein heavy chain1 is determined *in vitro* by at least one parameter selected from the group consisting of:

(a) rate of total protein transport through cellular Golgi apparatus;

(b) axonal transport;

(c) retrograde axonal transport;

(d) microtubule gliding rate;

(e) phagosome movement along microtubules;

(f) rate of intracellular trafficking of membranous organelles;

(g) nuclear migration rate;

(h) prometaphase chromosome movement.

9. The modified cytoplasmic dynein heavy chain1 polypeptide according to any one of claims 1 to 8 wherein expression of the protein within a non-human animal model heterozygous for the modified and wild type cytoplasmic dynein heavy chain1 gene results in the animal developing at least one of the following phenotypical features:

(a) epilepsy;

(b) myoclonic cramping;

(c) neuronal excitotoxicity;

(d) cell damage in hippocampus;

(e) cell damage in cerebellum;

(f) neurodegenerative disease;

(g) under-activity or undesirable activity of endogenous cytoplasmic dynein heavy chain1;

(h) under-expression, under-production or undesirable production of endogenous cytoplasmic dynein heavy chain1; and

(i) undesirable medical condition shown to be modulated by endogenous cytoplasmic dynein heavy chain1.

10. The modified cytoplasmic dynein heavy chain1 polypeptide according to claim 9 wherein the phenotypical features developed by said non-human animal model comprise at least one feature selected from the following group:

(a) myoclonic cramping of the fore limbs;

(b) myoclonic cramping of the hind limbs;

(c) cell damage in CA3 and CA4 sectors of hippocampus;

(d) cell damage in gyrus dentatus;

(e) neuronal damage in the upper layer of the cortex and in the Purkinje cell layer of the cerebellum;

(f) motor neuron impairment;

(g) Alzheimer's disease;

(h) Parkinson's disease;

(i) amyotropic lateral sclerosis;

(j) spinal muscular atrophy; and

(k) fiber type grouping in *Musculus tibialis anterior*.

11. A modified cytoplasmic dynein heavy chain1 polypeptide, wherein:

(a) the amino acid sequence of said modified cytoplasmic dynein heavy chain1 differs from the corresponding wild type sequence by substitution, deletion, or insertion of at least one amino acid residue in the wild type cytoplasmic dynein heavy chain1 sequence;

(b) the position of said amino acid residue in the cytoplasmic dynein heavy chain1 sequence is selected from the group consisting of:

(i) those positions at which, in each of the wild type cytoplasmic dynein heavy chain1 reference sequences, the identity of the wild type amino acid residue is restricted to conservative amino acid substitutions; and

(ii) those positions at which, in each of the wild type cytoplasmic dynein heavy chain1 reference sequences, the identity of the wild type amino acid residue is conserved; and

(c) said wild type cytoplasmic dynein heavy chain1 reference sequences consist of:

(i) SEQ ID NO:18 (*Homo sapiens*);

(ii) Genbank Accession No. NP_062099 (*Rattus norvegicus*); and

(iii) Genbank Accession No. NP_084514 (*Mus musculus*).

12. The modified cytoplasmic dynein heavy chain1 polypeptide of claim 11 wherein said the position of said amino acid residue is a position at which, in all of the wild type cytoplasmic dynein heavy chain1 reference sequences, the identity of the wild type amino acid residue is conserved.

13. The modified cytoplasmic dynein heavy chain1 polypeptide of any of claims 11 to 12, wherein said wild type cytoplasmic dynein heavy chain1 reference sequences consist of:

(i) SEQ ID NO:18 (*Homo sapiens*);

(ii) Genbank Accession No. NP_062099 (*Rattus norvegicus*);

(iii) Genbank Accession No. NP_084514 (*Mus musculus*);

(iv) Genbank Accession No. NP_523929 (*Drosophila melanogaster*); and

(v) Genbank Accession No. NP_084514 (*Caenorhabditis elegans*).

14. The modified cytoplasmic dynein heavy chain1 polypeptide of any of claims 11 to 13 wherein said amino acid residue corresponds to a residue selected from the group of conserved amino acid residues between Leu302 (302L) and Phe1140 (1140F) of SEQ ID NO:2 (*Mus musculus*) specified in Table 19.

15. The modified cytoplasmic dynein heavy chain1 polypeptide of any of claims 11 to 14 wherein said amino acid residue is positioned in a cytoplasmic dynein heavy chain1 domain capable of binding a subunit of the cytoplasmic dynein complex selected from the group consisting of:

(a) cytoplasmic dynein heavy chain1;

(b) cytoplasmic dynein intermediate chain;

(c) cytoplasmic dynein light intermediate chain; and

(d) cytoplasmic dynein light intermediate chain.

16. The modified cytoplasmic dynein heavy chain1 polypeptide of any of claims 11 to 15 wherein said amino acid residue is positioned in the cytoplasmic dynein heavy chain1 dimerization binding domain.

17. The modified cytoplasmic dynein heavy chain1 polypeptide of any of claims 11 to 16 wherein said amino acid residue is located in a sequence selected from the group consisting of:

(a) sequences encoded by cytoplasmic dynein heavy chain1 exon 13;

(b) SEQ ID NO:21;

(c) SEQ ID NO:23;

(d) sequences encoded by cytoplasmic dynein heavy chain1 exons 12 and13

(e) SEQ ID NO:22;

(f) SEQ ID NO:24.

18. The modified cytoplasmic dynein heavy chain1 polypeptide of any of claims 11 to 17 wherein said amino acid residue is located in a position corresponding to a residue selected from the group consisting of:

(a) in SEQ ID NO:2 (*Mus musculus*),

(i) residue 300 to residue 1140;

(ii) residue 416 to residue 701;

(iii) residue 649 to residue 800;

(b) in SEQ ID NO:18 (*Homo sapiens*);

(i) residue 302 to residue 1142;

(ii) residue 418 to residue 703;

(iii) residue 651 to residue 802.

19. The modified cytoplasmic dynein heavy chain1 polypeptide of claim 18 wherein said amino acid residue is located in a position corresponding to a residue selected from the group consisting of:

(a) in SEQ ID NO:2 (*Mus musculus*), residue 649 to residue 701;

(b) in SEQ ID NO:18 (*Homo sapiens*), residue 651 to residue 703.

20. The modified cytoplasmic dynein heavy chain1 polypeptide of any of claims 11 to 19, wherein the amino acid sequence of said modified cytoplasmic dynein heavy chain1 differs from the corresponding wild type sequence by substitution, deletion, or insertion of two or more of said amino acid residues in the wild type cytoplasmic dynein heavy chain1 sequence and wherein said amino acid residues are contiguous amino acid residues.

21. The modified cytoplasmic dynein heavy chain1 polypeptide of any of claims 11 to 20, wherein the amino acid sequence of said modified cytoplasmic dynein heavy chain1 differs from the corresponding wild type sequence by substitution, deletion, or insertion of at least ten of said amino acid residues.

22. The modified cytoplasmic dynein heavy chain1 polypeptide of any of claims 11 to 21, wherein the amino acid sequence of said modified cytoplasmic dynein heavy chain1 differs from the corresponding wild type sequence by substitution, deletion, or insertion of at least ten of said amino acid residues.

23. The modified cytoplasmic dynein heavy chain1 polypeptide of any of claims 11 to 18 and 20 to 22, wherein said amino acid residue is selected from the following group:

(a) a residue at a position within ten residues of position 1055 of the amino acid sequence as shown in SEQ ID NO:2;

(b) a residue at a position within ten residues of position 1057 of the amino acid sequence as shown in SEQ ID NO:18;

(c) a residue corresponding to one of the residues of the amino acid sequence

VEQYVKVWLQYQCLWDMQAEN.

24. The modified cytoplasmic dynein heavy chain1 polypeptide of any of claims 11 to 18 and 20 to 22, wherein said amino acid residue corresponds to a residue in SEQ ID NO:2 selected from the group consisting of:1035Y; 1036S; 1037A; 1038V; 1039M; 1040G; 1041I; 1042V; 1044E; 1045V; 1046E; 1047Q; 1048Y; 1049V; 1050K; 1052W; 1053L; 1054Q; 1055Y; 1056Q; 1058L; 1059W; D1060D; 1061M; 1062Q; 1063A; 1064E; and 1065N.

25. The modified cytoplasmic dynein heavy chain1 polypeptide of claim 24 wherein said amino acid residue corresponds to a residue in SEQ ID NO:2 selected from the group consisting of: 1044E; 1045V; 1046E; 1047Q; 1048Y;

1049V; 1050K; 1052W; 1053L; 1054Q; 1055Y; 1056Q; 1058L; 1059W; 1060D; 1061M; 1062Q; 1063A; 1064E; and 1065N.

26. The modified cytoplasmic dynein heavy chain1 polypeptide of claim 24 wherein said amino acid residue corresponds to a residue in SEQ ID NO:2 selected from the group consisting of: 1052W; 1053L; 1054Q; 1055Y; and 1056Q.

27. A modified cytoplasmic dynein heavy chain1 polypeptide wherein the modification is an amino acid substitution in the wild type cytoplasmic dynein heavy chain1 sequence at a position selected from the group consisting of:

(a) a position corresponding to position 1055 of the amino acid sequence as shown in SEQ ID NO:2; and

(b) a position corresponding to position 1057 of the amino acid sequence as shown in SEQ ID NO:19.

28. The modified cytoplasmic dynein heavy chain1 polypeptide according to any of claims 1 to 27 wherein the modified cytoplasmic dynein heavy chain1 polypeptide is a mammalian cytoplasmic dynein heavy chain1 polypeptide.

29. The modified cytoplasmic dynein heavy chain1 polypeptide according to claim 28 wherein the cytoplasmic dynein heavy chain1 polypeptide is selected from the group consisting of:

(a) human cytoplasmic dynein heavy chain1 polypeptide;

(b) murine cytoplasmic dynein heavy chain1 polypeptide;

(c) rat cytoplasmic dynein heavy chain1 polypeptide.

30. The modified cytoplasmic dynein heavy chain1 polypeptide of any of claims 1 to 29, wherein said modified cytoplasmic dynein heavy chain1 protein is a recombinant protein.

31. The modified cytoplasmic dynein heavy chain1 polypeptide of any of claims 1 to 30 wherein said substitution, deletion, or insertion of at least one amino acid residue in the wild type cytoplasmic dynein heavy chain1 sequence is located within a region of the polypeptide selected from the group consisting of:

(a) the region encoded by exon 12;

(b) the region encoded by exon 13;

(c) the cytoplasmic dynein heavy chain1 dimerization domain;

(d) a cytoplasmic dynein heavy chain1 binding domain for a subunit of the cytoplasmic dynein complex distinct from cytoplasmic dynein heavy chain1.

32. The modified cytoplasmic dynein heavy chain1 polypeptide of any of claims 1 to 31 wherein said deletion is of more than one amino acid residue in the wild type cytoplasmic dynein heavy chain1 sequence and extends into a region of the polypeptide selected from the group consisting of:

(a) exon 12;

(b) exon 13;

(c) the cytoplasmic dynein heavy chain1 dimerization domain;

(d) a cytoplasmic dynein heavy chain1 binding domain for a subunit of the cytoplasmic dynein complex distinct from cytoplasmic dynein heavy chain1.

33. The modified cytoplasmic dynein heavy chain1 polypeptide according to any of claims 1 to 32 wherein the amino acid substitution replaces a Tyr residue.

34. The modified cytoplasmic dynein heavy chain1 polypeptide according to any of claims 1 to 33 wherein said amino acid substitution is with an amino acid residue selected from the group consisting of Met, Leu, Ile, Val and Cys.

35. The modified cytoplasmic dynein heavy chain1 polypeptide according to claim 34 wherein the amino acid substitution is with a Cys residue.

36. The modified cytoplasmic dynein heavy chain1 polypeptide according to claim 35 wherein the modified cytoplasmic dynein heavy chain1 polypeptide has an amino acid sequence selected from the group consisting of SEQ ID NO:4 and SEQ ID NO:6.

37. A cytoplasmic dynein heavy chain1 polypeptide comprising the polypeptide according to any one of claims 1 to 36.

38. A murine cytoplasmic dynein heavy chain1 polypeptide having an amino acid sequence of SEQ ID NO:4.

39. A human cytoplasmic dynein heavy chain1 polypeptide having an amino acid sequence selected from the group consisting of:

(a) the amino acid sequence as shown in SEQ ID NO:6; and

(b) the amino acid sequence as shown in SEQ ID NO:18.

40. A cytoplasmic dynein heavy chain1 chimeric protein, comprising a cytoplasmic dynein heavy chain1 polypeptide according to any one of claims 1 to 39, conjugated or fused with a non-cytoplasmic dynein heavy chain1 polypeptide.

41. The cytoplasmic dynein heavy chain1 chimeric protein of claim 40, which comprises a cytoplasmic dynein heavy chain1 polypeptide according to any one of claims 37 to 39, conjugated or fused with a non-cytoplasmic dynein heavy chain1 polypeptide.

42. A monoclonal antibody capable of binding specifically to a cytoplasmic dynein heavy chain1 polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO:4 and SEQ ID NO:6 in preference to a

cytoplasmic dynein heavy chain1 polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO:2 and SEQ ID NO:18.

43. A monoclonal antibody capable of binding specifically to a cytoplasmic dynein heavy chain1 polypeptide having an amino acid sequence of SEQ ID NO:6 in preference to the cytoplasmic dynein heavy chain1 polypeptide of SEQ ID NO:18.

44. A composition comprising:

(a) a polypeptide selected from the group consisting of:

(i) the cytoplasmic dynein heavy chain1 polypeptide of any of claims 1 to 37;

(ii) the murine cytoplasmic dynein heavy chain1 polypeptide of claim 38;

(iii) the in-frame amino acid sequence derived from exon 12 of Dchc;

(iv) the in-frame amino acid sequence derived from exon 13 of Dchc;

(v) the in-frame amino acid sequence derived from exons 12 and 13 of Dchc;

(vi) the human cytoplasmic dynein heavy chain1 polypeptide of claim 39;

(vii) the cytoplasmic dynein heavy chain1 chimeric protein of any of claims 40 to 41; and

(viii) the monoclonal antibody of any of claims 42 to 43; and

(b) a pharmaceutically acceptable carrier.

45. The composition of claim 44 wherein the amino acid sequence of said polypeptide is selected from the group consisting of:

(a) SEQ ID NO:2;

(b) SEQ ID NO:18;

(c) SEQ ID NO:21;

(d) SEQ ID NO:22;

(e) SEQ ID NO:23; and

(f) SEQ ID NO:24.

46. A nucleic acid sequence encoding a cytoplasmic dynein heavy chain1 polypeptide selected from the group consisting of:

(a) the cytoplasmic dynein heavy chain1 polypeptide according to any one of claims 27 to 39; and

(b) the cytoplasmic dynein heavy chain1 chimeric protein of claim 40.

47. A polynucleotide, preferably isolated, comprising the nucleic acid sequence according to claim 46.

48. A polynucleotide, preferably isolated, comprising a nucleic acid sequence encoding a polypeptide comprising the amino acid sequence shown in SEQ ID NO:18.

49. A polynucleotide, preferably isolated, comprising a nucleic acid sequence encoding a polypeptide comprising an amino acid sequence selected from the following group:

(a) SEQ ID NO:21;

(b) SEQ ID NO:22;

(c) SEQ ID NO:23; and

(d) SEQ ID NO:24.

50. A nucleic acid vector comprising a polynucleotide selected from the following group:

(a) the polynucleotide of claim 47;

(b) the polynucleotide of claim 48;

(c) the polynucleotide of claim 49;

(d) a polynucleotide comprising a nucleic acid sequence encoding a polypeptide comprising the amino acid sequence SEQ ID NO:23; and

(e) a polynucleotide comprising a nucleic acid sequence encoding a polypeptide comprising the amino acid sequence SEQ ID NO:24.

51. An expression vector comprising the polynucleotide of any one of claims 47 to 48 operably linked to an expression control sequence suitable for directing transcription and translation of the polynucleotide in a selected host cell.

52. A host cell transformed with the vector of claim 51.

53. An antisense nucleic acid of length sufficient to inhibit the expression of a mutant cytoplasmic dynein heavy chain1 protein and total cellular cytoplasmic dynein heavy chain1 protein biological activity, wherein said antisense nucleic acid is complementary to a mammalian cytoplasmic dynein heavy chain1 nucleic acid sequence.

54. The antisense nucleic acid according to claim 53 wherein said mammalian cytoplasmic dynein heavy chain1 nucleic acid sequence is selected from the group consisting of human, bovine, equine, porcine, ovine, canine, feline, rat and murine cytoplasmic dynein heavy chain1 nucleic acid sequences.

55. The antisense nucleic acid according to any of claims 53 to 54 wherein said mammalian cytoplasmic dynein heavy chain1 nucleic acid sequence is selected from the group consisting of human cytoplasmic dynein heavy chain1 sequences corresponding to SEQ ID NO:6 and SEQ ID NO:18 and mouse cytoplasmic dynein heavy chain1 sequences corresponding to SEQ ID NO:2 and SEQ ID NO:4.

56. The antisense nucleic acid of any of claims 53 to 55, wherein the inhibitor of cytoplasmic dynein heavy chain1 biological activity inhibits a condition selected from the group consisting of:

(a) epilepsy;

(b) myoclonic cramping;

(c) neuronal excitotoxicity;

(d) cell damage in hippocampus;

(e) cell damage in cerebellum;

(f) neurodegenerative disease;

(g) under-activity or undesirable activity of endogenous cytoplasmic dynein heavy chain1;

(h) under-expression, under-production or undesirable production of endogenous cytoplasmic dynein heavy chain1; and

(i) undesirable medical condition shown to be modulated by endogenous cytoplasmic dynein heavy chain1.

57. The antisense nucleic acid according to claim 56, wherein the inhibitor of cytoplasmic dynein heavy chain1 biological activity inhibits a condition selected from the group consisting of:

(a) myoclonic cramping of the fore limbs;

(b) myoclonic cramping of the hind limbs;

(c) cell damage in CA3 and CA4 sectors of hippocampus;

(d) cell damage in gyrus dentatus;

(e) neuronal damage in the upper layer of the cortex and in the Purkinje cell layer of the cerebellum;

(f) motor neuron impairment;

(g) Alzheimer's disease;

(h) Parkinson's disease;

(i) amyotropic lateral sclerosis;

(j) spinal muscular atrophy;

(k) fiber type grouping in *Musculus tibialis anterior*.

58. The antisense nucleic acid of any of claims 53 to 56, wherein the inhibitor of cytoplasmic dynein heavy chain1 biological activity inhibits a condition selected from the group consisting of:

(a) over-activity or undesirable activity of endogenous cytoplasmic dynein heavy chain1;

(b) over-expression, over-production or undesirable production of endogenous cytoplasmic dynein heavy chain1; and

(c) undesirable medical condition shown to be modulated by endogenous cytoplasmic dynein heavy chain1.

59. The antisense nucleic acid according to claim 58, wherein the inhibitor of cytoplasmic dynein heavy chain1 biological activity inhibits a condition selected from the group consisting of:

(a) undesirable cell division;

(b) tumorigenesis.

60. A ribozyme comprising a hybridising region and a catalytic region wherein the hybridizing region is capable of hybridizing to at least part of a target mRNA sequence transcribed from a genomic gene corresponding to SEQ ID NO:1, 3, 5 or 17, wherein the catalytic domain is capable of cleaving the target mRNA sequence to reduce or inhibit a cytoplasmic dynein heavy chain1 mediated disorder.

61. A pharmaceutical composition comprising a nucleic acid molecule that inhibits or otherwise reduces a cytoplasmic dynein heavy chain1 mediated disorder wherein the nucleic acid comprises at least about ten nucleotides and hybridizes to or forms a heteroduplex with an mRNA molecule directed from a

gene encoding cytoplasmic dynein heavy chain1, the composition further comprising one or more pharmaceutically acceptable carriers.

62. The pharmaceutical composition of claim 61 for topical administration.

63. A medicament for the prevention, treatment or amelioration in a mammal of at least one medical condition selected from the group consisting of:

(a) epilepsy;

(b) myoclonic cramping;

(c) neuronal excitotoxicity;

(d) cell damage in hippocampus;

(e) cell damage in cerebellum;

(f) neurodegenerative disease;

(g) under-activity or undesirable activity of endogenous cytoplasmic dynein heavy chain1;

(h) under-expression, under-production or undesirable production of endogenous cytoplasmic dynein heavy chain1; and

(i) undesirable medical condition shown to be modulated by endogenous cytoplasmic dynein heavy chain1;

wherein said medicament comprises a polypeptide selected from the group consisting of:

(i) a cytoplasmic dynein heavy chain1 polypeptide;

(ii) the in-frame amino acid sequence derived from exon 12 of mouse or human Dchc;

(iii) the in-frame amino acid sequence derived from exon 13 of mouse or human Dchc;

(iv) the in-frame amino acid sequence derived from exons 12 and 13 of mouse or human Dchc;

(v) the chimeric protein according to any of claims 40 to 41; and

(vi) the monoclonal antibody according to any of claims 42 to 43.

64. The medicament according to claim 63 wherein said medical condition comprises at least one feature selected from the following group:

(a) myoclonic cramping of the fore limbs;

(b) myoclonic cramping of the hind limbs;

(c) cell damage in CA3 and CA4 sectors of hippocampus;

(d) cell damage in gyrus dentatus;

(e) neuronal damage in the upper layer of the cortex and in the Purkinje cell layer of the cerebellum;

(f) motor neuron impairment;

(g) Alzheimer's disease;

(h) Parkinson's disease;

(i) amyotropic lateral sclerosis;

(j) spinal muscular atrophy;

(k) fiber type grouping in *Musculus tibialis anterior*.

65. The medicament according to claims 63 to 64, wherein said polypeptide is a wild type mammalian cytoplasmic dynein heavy chain1 polypeptide.

66. The medicament according to claim 65, wherein said polypeptide is human cytoplasmic dynein heavy chain1 polypeptide.

67. The medicament according to claims 63 to 66, wherein said polypeptide has an amino acid sequence selected from the following group:

(i) SEQ ID NO:2;

(ii) SEQ ID NO:18;

(iii) SEQ ID NO:21;

(iv) SEQ ID NO:22;

(v) SEQ ID NO:23; and

(vi) SEQ ID NO:24.

68. A medicament for the prevention, treatment or amelioration in a mammal of at least one medical condition selected from the group consisting of:

(a) over-activity or undesirable activity of endogenous cytoplasmic dynein heavy chain1;

(b) over-expression, over-production or undesirable production of endogenous cytoplasmic dynein heavy chain1; and

(c) undesirable medical condition shown to be modulated by endogenous cytoplasmic dynein heavy chain1;

wherein the medicament comprises a polypeptide selected from the group consisting of:

(i) a cytoplasmic dynein heavy chain1 polypeptide according to any of claims 1 to 39;

(ii) the in-frame amino acid sequence derived from exon 12 of mouse or human Dchc;

(iii) the in-frame amino acid sequence derived from exon 13 of mouse or human Dchc;

(iv) the in-frame amino acid sequence derived from exons 12 and 13 of mouse or human Dchc;

(v) the chimeric protein according to any of claims 40 to 41; and

(vi) the monoclonal antibody according to any of claims 42 to 43.

69. The medicament according to claim 68 wherein said medical condition is selected from the following group:

(a) undesirable cell division;

(b) tumorigenesis.

70. The medicament according to any of claims 68 to 69, wherein said polypeptide has an amino acid sequence selected from the following group:

(a) SEQ ID NO:4;

(b) SEQ ID NO:6;

(c) SEQ ID NO:21;

(d) SEQ ID NO:22;

(e) SEQ ID NO:23; and

(f) SEQ ID NO:24.

71. The medicament according to any of claims 68 to 70, wherein said polypeptide is a dynein heavy chain1 polypeptide according to any of claims 11 to 39.

72. A medicament for the prevention, treatment or amelioration in a mammal of at least one medical condition selected from the group consisting of:

(a) epilepsy;

(b) myoclonic cramping;

(c) neuronal excitotoxicity;

(d) cell damage in hippocampus;

(e) cell damage in cerebellum;

(f) neurodegenerative disease;

(g) under-activity or undesirable activity of endogenous cytoplasmic dynein heavy chain1;

(h) under-expression, under-production or undesirable production of endogenous cytoplasmic dynein heavy chain1; and

(i) undesirable medical condition shown to be modulated by endogenous cytoplasmic dynein heavy chain1;

wherein the medicament comprises the polynucleotide of any of claims 47 to 49, or the vector of any one of claims 50 to 51.

73. The medicament according to claim 72 wherein said medical condition comprises at least one feature selected from the following group:

(a) myoclonic cramping of the fore limbs;

(b) myoclonic cramping of the hind limbs;

(c) cell damage in CA3 and CA4 sectors of hippocampus;

(d) cell damage in gyrus dentatus;

(e) neuronal damage in the upper layer of the cortex and in the Purkinje cell layer of the cerebellum;

(f) motor neuron impairment;

(g) Alzheimer's disease;

(h) Parkinson's disease;

(i) amyotropic lateral sclerosis;

(j) spinal muscular atrophy;

(k) fiber type grouping in *Musculus tibialis anterior*.

74. The medicament according to claim 73, wherein said polynucleotide comprises a nucleic acid sequence encoding a polypeptide comprising an amino acid sequence selected from the following group:

(a) SEQ ID NO:2;

(b) SEQ ID NO:18;

(c) SEQ ID NO:21;

(d) SEQ ID NO:22;

(e) SEQ ID NO:23; and

(f) SEQ ID NO:24.

75. A medicament for the prevention, treatment or amelioration in a mammal of at least one medical condition selected from the group consisting of:

(a) over-activity or undesirable activity of endogenous cytoplasmic dynein heavy chain1;

(b) over-expression, over-production or undesirable production of endogenous cytoplasmic dynein heavy chain1; and

(c) undesirable medical condition shown to be modulated by endogenous cytoplasmic dynein heavy chain1;

wherein the medicament comprises a polynucleotide selected from the group consisting of:

(i) a polynucleotide according to claim 47;

(ii) a polynucleotide comprising a nucleic acid sequence encoding an in-frame amino acid sequence selected from exon 12 of mouse or human Dchc;

(iii) a polynucleotide comprising a nucleic acid sequence encoding an in-frame amino acid sequence selected from exon 13 of mouse or human Dchc;

(iv) a polynucleotide comprising a nucleic acid sequence encoding an in-frame amino acid sequence selected from exons 12 and 13 of mouse or human Dchc.

76. The medicament according to claim 73, wherein said polynucleotide comprises a nucleic acid sequence encoding a polypeptide comprising an amino acid sequence selected from the following group:

(a) SEQ ID NO:4;

(b) SEQ ID NO:6;

(c) SEQ ID NO:21;

(d) SEQ ID NO:22;

(e) SEQ ID NO:23; and

(f) SEQ ID NO:24.

77. A medicament for the prevention, treatment or amelioration in a mammal of at least one medical condition selected from the group consisting of:

(a) over-activity or undesirable activity of endogenous cytoplasmic dynein heavy chain1;

(b) over-expression, over-production or undesirable production of endogenous cytoplasmic dynein heavy chain1; and

(c) undesirable medical condition shown to be modulated by endogenous cytoplasmic dynein heavy chain1;

wherein the medicament comprises a vector selected from the group consisting of:

(i) a nucleic acid vector comprising a polynucleotide encoding a polypeptide comprising an amino acid sequence selected from SEQ ID NO:4, 6, 21, 22, 23 and 24; and

(ii) an expression vector comprising a polynucleotide operably inked to an expression control sequence suitable for directing transcription and translation of said polynucleotide in a selected host cell, wherein said polynucleotide encodes a polypeptide comprising an amino acid sequence selected from SEQ ID NO:4, 6, 21, 22, 23 and 24.

78. A process for preparing a cytoplasmic dynein heavy chain1 polypeptide comprising:

(a) growing a culture of the host cell of claim 52 in a suitable culture medium; and

(b) recovering the cytoplasmic dynein heavy chain1 polypeptide from the culture.

79. A method for the prevention, treatment or amelioration of a cytoplasmic dynein heavy chain1-mediated medical condition in a mammalian subject,

particularly a human subject, comprising the step of administering to the subject a cytoplasmic dynein heavy chain1 polypeptide selected from the group consisting of:

(a) the modified cytoplasmic dynein heavy chain1 polypeptide of claims 1 to 10;

(b) the modified cytoplasmic dynein heavy chain1 polypeptide of claims 11 to 26;

(c) the modified cytoplasmic dynein heavy chain1 polypeptide of claims 27 to 36;

(d) the cytoplasmic dynein heavy chain1 polypeptide of claim 37; and

(e) the cytoplasmic dynein heavy chain1 polypeptide of claims 38 or 39.

80. A method of prevention, treatment or amelioration of a cytoplasmic dynein heavy chain1-mediated medical condition in a mammalian subject, particularly a human subject, comprising the step of administering to the subject a protein selected from the group consisting of:

(a) the chimeric protein of any of claims 40 to 41; and

(b) the monoclonal antibody of claim 42 to 43.

81. A method of preventing, treating or ameliorating a cytoplasmic dynein heavy chain1-mediated medical condition in a mammalian subject, particularly a human subject, comprising the step of administering to the subject a composition selected from the following group:

(a) the composition of claim 44; and

(b) the composition of claim 45.

82. A method of diagnosing in a mammalian subject, particularly a human subject, at least one of:

(a) cytoplasmic dynein heavy chain1-mediated medical condition;

(b) a susceptibility to develop a cytoplasmic dynein heavy chain1-mediated medical condition;

wherein the method comprises the steps of:

(i) isolating a biological sample from the subject;

(ii) comparing expression levels of cytoplasmic dynein heavy chain1 in the subject sample against a reference value.

83. The method of claim 82 wherein said reference value is obtained by performing the method with a wild type sample equivalent to the biological sample from the subject.

84. The method of claims 82 or 83 wherein a positive diagnosis is indicated by determining a cytoplasmic dynein heavy chain1 expression level in the subject sample that differs from that in the wild type sample by a factor selected from the group consisting of:

(a) expression in subject sample being less than 50% of expression in wild type sample;

(b) expression in subject sample being less than 20% of expression in wild type sample;

(c) expression in subject sample being less than 5% of expression in wild type sample;

and wherein the expression level of cytoplasmic dynein heavy chain1 in the subject sample is at least 0.5% of that in the wild type sample.

85. The method of any of claims 82 to 84, wherein said abnormal expression is delimited the alteration in expression of cytoplasmic dynein heavy chain1 is determined by detecting the existence of a mutation in a nucleic acid sequence

controlling the level of expression of the cytoplasmic dynein heavy chain1 polypeptide.

86. A method of diagnosing in a mammalian subject, particularly a human subject, at least one of:

(a) cytoplasmic dynein heavy chain1-mediated medical condition;

(b) a susceptibility to develop a cytoplasmic dynein heavy chain1-mediated medical condition;

wherein the method comprises the steps of:

(i) isolating a sample of nucleic acid from the subject; and

(ii) determining that said sample comprises a mutation in the nucleic acid sequence of a polynucleotide encoding the cytoplasmic dynein heavy chain1 polypeptide, wherein said mutation is responsible for a substitution, deletion or insertion of at least one amino acid residue in the encoded polypeptide.

87. The method of claim 86 wherein said method comprises the additional step of identifying said mutation.

88. The method of claim 87 wherein the method is capable of detecting a point mutation.

89. The method of claims 86 or 87 wherein the method comprises the additional step of determining that the cytoplasmic dynein heavy chain1 encoded by said polynuclotide is a modified cytoplasmic dynein heavy chain1 polypeptide selected from the group consisting of:

(a) the modified cytoplasmic dynein heavy chain1 polypeptide of claims 1 to 10;

(b) the modified cytoplasmic dynein heavy chain1 polypeptide of claims 11 to 26;

(c) the modified cytoplasmic dynein heavy chain1 polypeptide of claims 27 to 36.

90. The method of any of claims 86 to 89 wherein the method includes the additional step of amplification and subsequent sequencing of nucleic acid, and said mutation is identified by the sequence of the amplified nucleic acid.

91. The method of any of claims 86 to 90, wherein said method comprises the additional step of confirming that said mutation is associated with at least one of:

(a) cytoplasmic dynein heavy chain1-mediated medical condition;

(b) a susceptibility to develop a cytoplasmic dynein heavy chain1-mediated medical condition;

wherein said confirmation is obtained by generating a non-human animal model selected from the group consisting of:

(i) a non-human animal model expressing the corresponding mutation in the animal's cytoplasmic dynein heavy chain1, as a heterozygote;

(ii) a non-human animal model expressing the corresponding mutation in the animal's cytoplasmic dynein heavy chain1, as a homozygote;

(iii) a transgenic non-human animal model expressing the corresponding mutation in human cytoplasmic dynein heavy chain1, as a heterozygote; and

(iv) a transgenic non-human animal model expressing the corresponding mutation in human cytoplasmic dynein heavy chain1, as a heterozygote;

and observing the phenotype of said non-human animal.

92. The method of any of claims 86 to 91, wherein said method comprises the additional step of confirming that said mutation is associated with at least one of:

(a) cytoplasmic dynein heavy chain1-mediated medical condition;

(b) a susceptibility to develop a cytoplasmic dynein heavy chain1-mediated medical condition;

wherein said confirmation is obtained by an analysis selected from the group consisting of:

(i) a structural analysis of cytoplasmic dynein heavy chain1 comprising said mutation;

(ii) assaying a biological function of cytoplasmic dynein heavy chain1 comprising said mutation.

93. The method of claim 92 wherein said analysis comprises at least one method selected from the group consisting of:

(a) assaying whether the cytoplasmic dynein heavy chain1 comprising said mutation is capable of dimerization;

(b) assaying whether the cytoplasmic dynein heavy chain1 comprising said mutation binds a recombinantly produced peptide corresponding to the dimerization domain of cytoplasmic dynein heavy chain1, preferably corresponding to the dimerization domain of human cytoplasmic dynein heavy chain1;

(c) assaying whether the cytoplasmic dynein heavy chain1 comprising said mutation binds other components of the dynein complex selected from the group comprsing:

(i) dynein intermediate chain;

(ii) dynein light intermediate chain;

(iii) dynein light chain;

(iv) dynactin;

(v) dynamitin;

(d) assaying whether the cytoplasmic dynein heavy chain1 comprising said mutation is capable of integration into an intact dynein complex;

(e) assaying whether formation of intact dynein complex is inhibited in the presence of the cytoplasmic dynein heavy chain1 comprising said mutation;

(f) assaying whether the cytoplasmic dynein heavy chain1 comprising said mutation is capable of actin movement; and

(g) assaying whether the cytoplasmic dynein heavy chain1 comprising said mutation is capable of axonal transport.

94. The method of any of claims 86 to 93, wherein said method comprises database comparison, wherein the database comprises mutations in cytplasmic dynein heavy chain 1 that are associated with at least one medical condition selected from the group consisting of:

(a) epilepsy;

(b) myoclonic cramping;

(c) neuronal excitotoxicity;

(d) cell damage in hippocampus;

(e) cell damage in cerebellum;

(f) neurodegenerative disease;

(g) under-activity or undesirable activity of endogenous cytoplasmic dynein heavy chain1;

(h) under-expression, under-production or undesirable production of endogenous cytoplasmic dynein heavy chain1; and

(i) undesirable medical condition shown to be modulated by endogenous cytoplasmic dynein heavy chain1.

95. A database according to claim 94 wherein said database comprises mutations in cytplasmic dynein heavy chain 1 that are associated to at least one feature selected from the group consisting of:

(a) myoclonic cramping of the fore limbs;

(b) myoclonic cramping of the hind limbs;

(c) cell damage in CA3 and CA4 sectors of hippocampus;

(d) cell damage in gyrus dentatus;

(e) neuronal damage in the upper layer of the cortex and in the Purkinje cell layer of the cerebellum;

(f) motor neuron impairment;

(g) Alzheimer's disease;

(h) Parkinson's disease;

(i) amyotropic lateral sclerosis;

(j) spinal muscular atrophy;

(k) fiber type grouping in *Musculus tibialis anterior*.

96. The method of any of claims 86 to 95 wherein the mutation is located the nucleic acid sequence encoding cytoplasmic dynein heavy chain 1, wherein cytoplasmic dynein heavy chain 1 is selected from SEQ ID NO:17.

97. The method of any of claims 86 to 96 wherein the mutation is located in a selected region of the nucleic acid sequence encoding cytoplasmic dynein heavy chain 1, wherein said selected region is selected from the group of:

(a) exon 12;

(b) exon 12 and exon 13;

(c) the dimerization binding site of cytoplasmic dynein heavy chain1.

98. The method of claim 97 wherein the mutation is located in cytoplasmic dynein heavy chain1, wherein said selected region comprises the amino acid sequences, selected from the group of:

(a) SEQ ID NO:23

(b) SEQ ID NO:24

(c) residues 302 to residues 1142 in SEQ ID NO:18.

99. The method of any of claims 86 to 98, wherein said medical condition is a neurodegenerative disease.

100. The method of claim 99 wherein said neurodegenerative disease is a progressive neurodegenerative disease and is selected from the group of Alzheimer's disease, Parkinson's disease, amyotropic lateral sclerosis and spinal muscular atrophy.

101. A method of gene delivery and expression in a target cell of a mammal, comprising the step of introducing a viral vector into the target cell, wherein the viral vector is derived from a virus that has a low replicative efficiency in the target cell and has at least one insertion site containing a nucleic acid of any of claims 47, 53, 54, 55, 56, 57, 58 and 59, and the nucleic acid is operably linked to a promoter capable of expression in the host.

102. The method of claim 101, wherein the viral vector is a non-lytic viral vector.

103. A method of gene delivery and expression in a target cell of a mammal comprising the steps of:

(a) providing an isolated nucleic acid fragment of claims 47, 53, 54, 55, 56, 57, 58 and 59;

(b) selecting a viral vector derived from a virus that has a low replicative efficiency in the target cell, wherein the vector has at least one insertion site for insertion of said isolated nucleic acid fragment operably linked to a promoter capable of expression in the target cells;

(c) inserting the isolated nucleic acid fragment into the insertion site; and

(d) introducing the vector into said target cell wherein said gene is expressed at detectable levels.

104. The method of any of claims 101 to 103 wherein the virus is selected from the group consisting of retrovirus, adenovirus, iridoviruses, coronaviruses, togaviruses, caliciviruses and picornaviruses.

105. The method of any of claims 101 to 104 wherein the virus is selected from the group consisting of retrovirus, adenovirus, and pox virus.

106. The method of claim 105 wherein the pox virus is vaccinia.

107. The method of any of claims 101 to 106, wherein the virus is a strain that has been genetically modified or selected to be non-virulent in a host.

108. A non-human animal model expressing a modified cytoplasmic dynein heavy chain1 polypeptide selected from the group consisting of:

(a) the modified cytoplasmic dynein heavy chain1 polypeptide of claims 1 to 10;

(b) the modified cytoplasmic dynein heavy chain1 polypeptide of claims 11 to 26;

(c) the modified cytoplasmic dynein heavy chain1 polypeptide of claims 27 to 36.

109. The non-human animal model according to claim 108 which is a mammalian non-human animal model.

110. The non-human animal model according to claim 109 which is selected from the group consisting of bovine, equine, porcine, ovine, canine, feline, rat and murine non-human animal models.

111. The non-human animal model according to any one of claims 108 to 110 wherein the modified cytoplasmic dynein heavy chain1 is encoded by a nucleic acid sequence which is heterozygous in the animal model.

112. The non-human animal model according to any one of claims 108 to 111 wherein the animal exhibits at least one of the following phenotypical features:

(a) epilepsy;

(b) myoclonic cramping;

(c) neuronal excitotoxicity;

(d) cell damage in hippocampus;

(e) cell damage in cerebellum;

(f) neurodegenerative disease;

(g) under-activity or undesirable activity of endogenous cytoplasmic dynein heavy chain1;

(h) under-expression, under-production or undesirable production of endogenous cytoplasmic dynein heavy chain1; and

(i) undesirable medical condition shown to be modulated by endogenous cytoplasmic dynein heavy chain1.

113. The non-human animal model according to claim 112 wherein the phenotypical features exhibited by the animal include at least one feature selected from the following group:

(a) myoclonic cramping of the fore limbs;

(b) myoclonic cramping of the hind limbs;

(c) cell damage in CA3 and CA4 sectors of hippocampus;

(d) cell damage in gyrus dentatus;

(e) neuronal damage in the upper layer of the cortex and in the Purkinje cell layer of the cerebellum;

(f) motor neuron impairment;

(g) Alzheimer's disease;

(h) Parkinson's disease;

(i) amyotropic lateral sclerosis;

(j) spinal muscular atrophy; and

(k) fiber type grouping in *Musculus tibialis anterior*.

114. A transgenic non-human animal model expressing a human cytoplasmic dynein heavy chain1.

115. A transgenic non-human animal model according to claim 114 wherein the human cytoplasmic dynein heavy chain1 has an amino acid sequence selected from SEQ ID NO:6 or SEQ ID NO:18.

116. The non-human animal model according to any of claims 108 to 115 wherein the animal is a mouse.

117. An animal model according to any one of claims 108 to 116 utilized for the study of diseases or symptoms associated with cytoplasmic dynein heavy chain1 activity deficiency.

118. An animal model according to any one of claims 108 to 116 utilized for the identification of early diagnostic markers for diseases associated with cytoplasmic dynein heavy chain1 activity deficiency.

119. An animal model according to any one of claims 108 to 116 utilized for monitoring the activity of agents useful in the prevention or treatment of

diseases or symptoms associated with cytoplasmic dynein heavy chain1 activity deficiency.

120. An animal model according to any one of claims 108 to 116 utilized as a model system for testing agents suspected of promoting or aggravating diseases associated with cytoplasmic dynein heavy chain1 activity deficiency by administering or applying such agents to the model and monitoring at least one effect thereof.

121. A primary cell or cell lines derived from the animal model according to any one of claims 108 to 116.

122. A method of identifying a protein or nucleic acid marker indicative of an increased risk of a mammalian subject, particularly a human subject, of developing a neurodegenerative disease, said method comprising the step of analyzing a test sample derived from said subject for the presence of a difference compared to a similar test sample if derived from a subject of the same species unaffected by or known not to be at risk of developing said disease, wherein said difference is indicative of the presence of a mutation in an allele of a gene coding for a protein, which is a subunit of the dynactin/dynein complex.

123. A method of identifying a protein or nucleic acid marker indicative of an association of a neurodegenerative disease in a mammalian subject, particularly a human subject, with a mutation in an allele of a gene coding for a protein, which is a subunit of the dynactin/dynein complex, said method comprising the step of analyzing a test sample derived from said subject for the presence of a difference compared to a similar test sample if derived from a subject of the same species, unaffected by or known not to be at risk of developing said disease, wherein said difference is indicative of the presence of a mutation in an allele of a gene coding for a protein, which is a subunit of the dynactin/dynein complex.

124. The method of claim 122 or 123, wherein said test sample is analyzed for a difference compared to similar test samples if derived from a group of mammalian subjects of the same species as said subject, which subjects are unaffected by, or known not to be at risk of developing, said neurodegenerative disease.

125. The method according to any one of claims 122 to 124, wherein said mammalian subject whose test sample is analyzed has a neurodegenerative disease or is known or suspected to be at risk of developing a neurodegenerative disease.

126. The method of any one of claims 122 to 125, further comprising the step of obtaining said similar test sample or said similar test samples from said mammalian subject or group of mammalian subjects.

127. The method according to any one of claims 122 to 126, wherein said neurodegenerative disease is selected from the group consisting of Alzheimer's Disease, Parkinson's Disease, Huntington's Disease.

128. The method according to any one of claims 122 to 126, wherein said neurodegenerative disease is a motorneuron degenerative disease.

129. The method according to claim 128, wherein said motorneuron degenerative disease is selected from the group consisting of Amyotrophic Lateral Sclerosis, Spinal Muscular Atrophy, Bulbo-Spinal Muscular Atrophy, Progressive Bulbar Palsy, Progressive Muscular Atrophy, and Primary Lateral Sclerosis.

130. The method according to any one of claims 122 to 129, wherein said test sample is a nucleic acid sample.

131. The method according to claim 130, wherein said nucleic acid is selected from the group consisting of mRNA, cDNA and genomic DNA.

132. The method according to any of claims 130 or 131, wherein the nucleic acid is selected from the group consisting of nucleic acids coding for the cytoplasmic dynein heavy chain 1, e.g. SEQ ID NOS.: 28 or 29, the cytoplasmic dynein intermediate chain 1, e.g. SEQ ID NOS.: 30 or 31, the cytoplasmic dynein intermediate chain 2, e.g. SEQ ID NOS.: 32 or 33, the cytoplasmic dynein light intermediate chain 1, e.g. SEQ ID NOS.: 34 or 35, the cytoplasmic dynein light intermediate chain 2, e.g. SEQ ID NOS.: 36 or 37; the cytoplasmic dynein 10 kDa light chain, e.g. SEQ ID NOS.: 38 or 39, the cytoplasmic dynein light chain Tctex 1, e.g. SEQ ID NOS.: 40 or 41, the cytoplasmic dynein light chain 2B, e.g. SEQ ID NO.: 42, DCTN 1, e.g. SEQ ID NOS.: 43 or 44, DCTN 2, e.g. SEQ ID NOS.: 159 or 45, DCTN 3, e.g. SEQ ID NOS.: 46 or 47, DCTN 4, e.g. SEQ ID NOS.: 48 or 49, DCTN 5, e.g. SEQ ID NO.: 50, DCTN 6, e.g. SEQ ID NOS.: 51 or 52, ARP1, e.g. SEQ ID NOS.: 53 or 54, ARP11, e.g. SEQ ID NOS.: 55 or 56, HAP1, e.g. SEQ ID NOS.: 57 or 58, and CLIP-170, e.g. SEQ ID NOS.: 59 or 60, preferably the cytoplasmic dynein heavy chain 1, cytoplasmic dynein intermediate chain 1, cytoplasmic dynein intermediate chain 2, and/or DCTN 1, e.g. according to the above-mentioned corresponding SEQ ID NOS.

133. The method according to any of claims 122 to 132, wherein the step of analyzing said nucleic acid sample comprises amplifying at least a portion of its nucleic acid via the polymerase chain reaction, and optionally also amplifying via the polymerase chain reaction at least a portion of the nucleic acid of said similar sample or said similar samples.

134. The method according to any of claims 122 to 133, wherein the step of analyzing further comprises the step of determining whether said allele is homozygous or heterozygous with respect to said mutation.

135. The method according to claim 122 or 134, wherein the step of analyzing further comprises the separation of the amplified portion of said sample and optionally said similar sample or said similar samples by electrophoresis.

136. The method according to any of claims 122 to 135, wherein the step of analyzing comprises the partial or complete determination of the sequence of the nucleic acid or the amplified portion of the nucleic acid of said sample, and optionally also of the nucleic acid or the amplified portion of the nucleic acid of said similar sample or said similar samples.

137. The method according to any one of claims 122 to 129, wherein said test sample is a protein sample.

138. The method according to claim 137, wherein said protein sample comprises a protein selected from the group consisting of the cytoplasmic dynein heavy chain 1, e.g. encoded by SEQ ID NOS.: 28 or 29, the cytoplasmic dynein intermediate chain 1, e.g. encoded by SEQ ID NOS.: 30 or 31, the cytoplasmic dynein intermediate chain 2, e.g. encoded by SEQ ID NOS.: 32 or 33, the cytoplasmic dynein light intermediate chain 1, e.g. encoded by SEQ ID NOS.: 34 or 35, the cytoplasmic dynein light intermediate chain 2, e.g. encoded by SEQ ID NOS.: 36 or 37; the cytoplasmic dynein 10 kDa light chain, e.g. encoded by SEQ ID NOS.: 38 or 39, the cytoplasmic dynein light chain Tctex 1, e.g. encoded by SEQ ID NOS.: 40 or 41, the cytoplasmic dynein light chain 2B, e.g. encoded by SEQ ID NO.: 42, DCTN 1, e.g. encoded by SEQ ID NOS.: 43 or 44, DCTN 2, e.g. encoded by SEQ ID NOS.: 159 or 45, DCTN 3, e.g. encoded by SEQ ID NOS.: 46 or 47, DCTN 4, e.g. encoded by SEQ ID NOS.: 48 or 49, DCTN 5, e.g. encoded by SEQ ID NO.: 50, DCTN 6, e.g. encoded by SEQ ID NOS.: 51 or 52, ARP1, e.g. encoded by SEQ ID NOS.: 53 or 54, ARP11, e.g. encoded by SEQ ID NOS.: 55 or 56, HAP1, e.g. encoded by SEQ ID NOS.: 57 or 58, and CLIP-170, e.g. encoded by SEQ ID NOS.: 59 or 60, preferably the cytoplasmic dynein heavy chain 1, cytoplasmic dynein intermediate chain 1, cytoplasmic dynein intermediate chain 2, and/or DCTN 1, e.g. encoded by the above-mentioned corresponding SEQ ID NOS.

139. The method according to any one of claims 122 to 138, wherein said mutation selectively affects cell types associated with or suspected to be involved in a neurodegenerative disease.

140. The method according to any one of claims 122 to 139, wherein said mutation selectively affects motorneurons, preferably α-motorneurons.

141. The method according to any of claims 122 to 140, wherein said mutation affects a cellular process selected from the group of processes consisting of neuronal axonal transport, cellular transport, proliferation, differentiation and apoptosis.

142. The method according to any of claims 122 to 141, wherein said mutation leads to a disruption of, or alteration in the functional interaction within the dynactin/dynein complex in neurons, preferably in motorneurons.

143. The method according to any one of claims 122 to 142, wherein said mutation results in a deletion or substitution by another amino acid of an amino acid encoded by said allele, or an insertion of additional amino acids not normally present in the amino acid sequence of the protein encoded by said allele.

144. The method according to claim 143, wherein said deletion, substitution, or insertion is encoded by both alleles of the gene coding for said protein.

145. The method according to claim 143 or 144, wherein said deletion, substitution, or insertion of the amino acid occurs in an evolutionary conserved region of said protein.

146. The method according to any of claims 122 to 145, wherein said mutation results in the substitution of an amino acid which is identical between the corresponding mouse and human, preferably between the corresponding mouse, rat, and human protein encoded by said allele, by another amino acid.

147. The method according to any one of claims 143 to 146, wherein said amino acid is substituted by a naturally occurring amino acid.

148. The method according to any of claims 143 to 147, wherein said amino acid is encoded by a codon within the open reading frame of a nucleic acid sequence selected from the group consisting of SEQ ID NOS.: 70 to 112 or SEQ ID NOS.: 114 to 158.

149. The method according to any of claims 143 to 148, wherein said amino acid is located in a domain of said protein, which is capable of binding to another subunit of the dynactin/dynein complex.

150. The method according to claim 149, wherein said domain is defined by an amino acid sequence selected from the group of sequences consisting of

in case the protein is mouse cytoplasmic dynein intermediate chain 1 (SEQ ID NO.: 61):

i) amino acids 147-157;

ii) amino acid 243-314;

iii) amino acids 140-157; and

amino acids 1-123;

in case the protein is human cytoplasmic dynein intermediate chain 1 (SEQ ID NO.: 62):

v) amino acids 164-174;

vi) amino acids 260-331;

vii) amino acids 157-174; and

viii) amino acids 1-140;

in case the protein is mouse cytoplasmic dynein intermediate chain 2 (SEQ ID NO.: 64):

i) amino acids 1-123;

ii) amino acids 122-139;

iii) amino acids 129-130; and

iv) amino acids 226-297;

in case the protein is human cytoplasmic dynein intermediate chain 2 (SEQ ID NO.: 65):

v) amino acids 155-165;

vi) amino acids 252-323;

vii) amino acids 148-165; and

viii) amino acids 1-149;

in case the protein is mouse DCTN 1 (SEQ ID NO.: 67):

i) amino acids 39-150;

ii) amino acids 1006-1021; and

iii) amino acids 133-899: or

in case the protein is human DCTN1 (SEQ ID NO.: 68):

iv) amino acids 39-150;

v) amino acids 1006-1021; and

vi) amino acids 133-899.

151. The method according to claim 150, wherein

a) if the protein is cytoplasmic dynein intermediate chain 1 (SEQ ID NO.: 61 or 62), said amino acid is any one of the amino acids specified in Table 20;

b) if the protein is cytoplasmic dynein intermediate chain 2 (SEQ ID NO.: 64 or 65), said amino acid is any one of the amino acids specified in Table 21;

c) if the protein is DCTN 1 (SEQ ID NO.: 67 or 68), said amino acid is any one of the amino acids specified in Table 22.

152. A method for identifying a predisposition of a mammalian subject, particularly a human subject, for developing a neurodegenerative disease, said method comprising the step of determining whether a test sample derived from said subject indicates the presence of a mutation in an allele of a gene coding for a protein, which is a subunit of the dynactin/dynein complex, indicative of an increased risk of said subject of developing said neurodegenerative disease.

153. The method according to claim 152, further comprising the step of assigning a certain risk of developing said neurodegenerative disease to said subject.

154. A method for determining whether a neurodegenerative disease in a mammalian subject, particularly a human subject, is associated with a mutation in an allele of a gene coding for a protein, which is a subunit of the dynactin/dynein complex, said method comprising the step of determining whether a test sample derived from said subject indicates the presence of a mutation in an allele of a gene coding for said protein.

155. The method according to any of claims 152 to 154, wherein said neurodegenerative disease is selected from the group consisting of Alzheimer's Disease, Parkinson's Disease, and Huntington's Disease.

156. The method according to any one of claims 152 to 154, wherein said neurodegenerative disease is a motorneuron degenerative disease.

157. The method according to claim 156, wherein said motorneuron degenerative disease is selected from the group consisting of: Amyotrophic Lateral Sclerosis, Spinal Muscular Atrophy, Bulbo-Spinal Muscular Atrophy, Progressive Bulbar Palsy, Progressive Muscular Atrophy, and Primary Lateral Sclerosis.

158. The method according to any one of claims 152 to 157, wherein said test sample is a nucleic acid sample.

159. The method according to claim 158, wherein said nucleic acid is selected from the group consisting of mRNA, cDNA and genomic DNA.

160. The method according to claim 158 or 159, wherein the nucleic acid is selected from the group consisting of nucleic acids coding for the cytoplasmic dynein heavy chain 1, e.g. SEQ ID NOS.: 28 or 29, the cytoplasmic dynein intermediate chain 1, e.g. SEQ ID NOS.: 30 or 31, the cytoplasmic dynein intermediate chain 2, e.g. SEQ ID NOS.: 32 or 33, the cytoplasmic dynein light intermediate chain 1, e.g. SEQ ID NOS.: 34 or 35, the cytoplasmic dynein light intermediate chain 2, e.g. SEQ ID NOS.: 36 or 37; the cytoplasmic dynein 10 kDa light chain, e.g. SEQ ID NOS.: 38 or 39, the cytoplasmic dynein light chain Tctex 1, e.g. SEQ ID NOS.: 40 or 41, the cytoplasmic dynein light chain 2B, e.g. SEQ ID NO.: 42, DCTN 1, e.g. SEQ ID NOS.: 43 or 44, DCTN 2, e.g. SEQ ID NOS.: 159 or 45, DCTN 3, e.g. SEQ ID NOS.: 46 or 47, DCTN 4, e.g. SEQ ID NOS.: 48 or 49, DCTN 5, e.g. SEQ ID NO.: 50, DCTN 6, e.g. SEQ ID NOS.: 51 or 52, ARP1, e.g. SEQ ID NOS.: 53 or 54, ARP11, e.g. SEQ ID NOS.: 55 or 56, HAP1, e.g. SEQ ID NOS.: 57 or 58, and CLIP-170, e.g. SEQ ID NOS.: 59 or 60, preferably the cytoplasmic dynein heavy chain 1, cytoplasmic dynein intermediate chain 1, cytoplasmic dynein intermediate chain 2, and/or DCTN 1, e.g. according to the above-mentioned corresponding SEQ ID NOS.

161. The method according to any one of claims 152 to 157, wherein said test sample is a protein sample.

162. The method of claim 161, wherein said protein sample comprises a protein selected from the group consisting of the cytoplasmic dynein heavy chain 1, e.g. encoded by SEQ ID NOS.: 28 or 29, the cytoplasmic dynein intermediate chain 1, e.g. encoded by SEQ ID NOS.: 30 or 31, the cytoplasmic dynein intermediate chain 2, e.g. encoded by SEQ ID NOS.: 32 or 33, the cytoplasmic dynein light intermediate chain 1, e.g. encoded by SEQ ID NOS.: 34 or 35, the cytoplasmic dynein light intermediate chain 2, e.g. encoded by SEQ ID NOS.: 36 or 37; the cytoplasmic dynein 10 kDa light chain, e.g. encoded by SEQ ID

NOS.: 38 or 39, the cytoplasmic dynein light chain Tctex 1, e.g. encoded by SEQ ID NOS.: 40 or 41, the cytoplasmic dynein light chain 2B, e.g. encoded by SEQ ID NO.: 42, DCTN 1, e.g. encoded by SEQ ID NOS.: 43 or 44, DCTN 2, e.g. encoded by SEQ ID NOS.: 159 or 45, DCTN 3, e.g. encoded by SEQ ID NOS.: 46 or 47, DCTN 4, e.g. encoded by SEQ ID NOS.: 48 or 49, DCTN 5, e.g. encoded by SEQ ID NO.: 50, DCTN 6, e.g. encoded by SEQ ID NOS.: 51 or 52, ARP1, e.g. encoded by SEQ ID NOS.: 53 or 54, ARP11, e.g. encoded by SEQ ID NOS.: 55 or 56, HAP1, e.g. encoded by SEQ ID NOS.: 57 or 58, and CLIP-170, e.g. encoded by SEQ ID NOS.: 59 or 60, preferably the cytoplasmic dynein heavy chain 1, cytoplasmic dynein intermediate chain 1, cytoplasmic dynein intermediate chain 2, and/or DCTN 1, e.g. encoded by the above-mentioned corresponding SEQ ID NOS.

163. The method according to any one of claims 152 to 162, wherein said mutation selectively affects cell types associated with or suspected to be involved in developing a neurodegenerative disease.

164. The method according to any one of claims 152 to 163, wherein said mutation selectively affects motorneurons, preferably α-motorneurons.

165. The method according to any of claims 152 to 164, wherein said mutation affects a cellular process selected from the group of processes consisting of neuronal axonal transport, cellular transport, proliferation, differentiation and apoptosis.

166. The method according to any of claims 152 to 165, wherein said mutation leads to a disruption of, or alteration in the functional interaction within the dynactin/dynein complex in neurons, preferably in motorneurons.

167. The method according to any one of claims 152 to 166, wherein said mutation results in a deletion or substitution by another amino acid of an amino acid encoded by said allele, or an insertion of additional amino acids not normally present in the amino acid sequence of said protein, encoded by said allele.

168. The method according to claim 167, wherein said deletion, substitution, or insertion is encoded by both alleles of the gene coding for said protein.

169. The method according to any of claims 167 or 168, wherein said deletion, substitution, or insertion occurs in an evolutionary conserved region of said protein.

170. The method according to any of claims 152 to 169, wherein said mutation results in the substitution of an amino acid which is identical between the corresponding mouse and human protein, preferably between the corresponding mouse, rat, and human protein encoded by said allele, by another amino acid.

171. The method according to any of claims 167 to 170, wherein said amino acid is substituted by a naturally occurring amino acid.

172. The method according to any of claims 167 to 171, wherein said amino acid is encoded by a codon within the open reading frame of a nucleic acid sequence selected from the group consisting of SEQ ID NO.: 70-112 or SEQ ID NO.: 114-158.

173. The method according to any of claims 167 to 172, wherein said amino acid is located in a domain of said protein, which is capable of binding to another subunit of the dynactin/dynein complex.

174. The method according to claim 173, wherein said domain is defined by an amino acid sequence selected from the group of sequences consisting of

in case the protein is mouse cytoplasmic dynein intermediate chain 1 (SEQ ID NO.: 61):

i) amino acids 147-157;

ii) amino acid 243-314;

iii) amino acids 140-157; and

iv) amino acids 1-123;

in case the protein is human cytoplasmic dynein intermediate chain 1 (SEQ ID NO.: 62):

v) amino acids 164-174;

vi) amino acids 260-331;

vii) amino acids 157-174; and

viii) amino acids 1-140;

in case the protein is mouse cytoplasmic dynein intermediate chain 2 (SEQ ID NO.: 64):

i) amino acids 1-123;

ii) amino acids 122-139;

iii) amino acids 129-130; and

iv) amino acids 226-297;

in case the protein is human cytoplasmic dynein intermediate chain 2 (SEQ ID NO.: 65):

v) amino acids 155-165;

vi) amino acids 252-323;

vii) amino acids 148-165; and

viii) amino acids 1-149;

in case the protein is mouse DCTN 1 (SEQ ID NO.: 67):

i) amino acids 39-150;

ii) amino acids 1006-1021; and

iii) amino acids 133-899: or

in case the protein is human DCTN1 (SEQ ID NO.: 68):

iv) amino acids 39-150;

v) amino acids 1006-1021; and

vi) amino acids 133-899.

175. The method according to claim 174, wherein

a) if the protein is cytoplasmic dynein intermediate chain 1 (SEQ ID NOS.: 61 or 62), said amino acid is any one of the amino acids specified in Table 20;

b) if the protein is cytoplasmic dynein intermediate chain 2 (SEQ ID NOS.: 64 or 65), said amino acid is any one of the amino acids specified in Table 21;

c) if the protein is DCTN 1 (SEQ ID NOS.: 67 or 68), said amino acid is any one of the amino acids specified in Table 22.

176. An oligonucleotide suitable for identifying a mutation in an allele of a gene coding for a protein, which is a subunit of the dynactin/dynein complex.

177. An oligonucleotide according to claim 176, the nucleotide sequence of which corresponds to a nucleotide sequence within said allele, which contains a mutation as defined in any of claims 139 to 151.

178. An oligonucleotide according to claim 176 or 177, which is suitable for hybridizing to the nucleic acid of said allele or a portion of its nucleic acid under stringent conditions.

179. An oligonucleotide according to any of claims 176 to 178, which is suitable as primer for amplifying the nucleic acid of said allele or a portion of its nucleic acid.

180. A kit for identifying a predisposition of a mammalian subject, particularly a human subject, for developing a neurodegenerative disease, or for identifying an association of a neurodegenerative disease of said subject with a mutation in an allele coding for a protein, which is a subunit of the dynactin/dynein complex, said kit comprising one or more oligonucleotides according to any of claims 176 to 178.

181. A kit for identifying a predisposition of a mammalian subject, particularly a human subject, for developing a neurodegenerative disease or for an association of a neurodegenerative disease of said subject with a mutation in an allele coding for a protein, which is a subunit of the dynactin/dynein complex, said kit comprising at least two oligonucleotides according to claim 179.

182. The kit according to claims 180 or 181, further comprising instructions to use the oligonucleotide or the oligonucleotides for identifying said predisposition in said subject or said association of the neurodegenerative disease of said subject with said mutation.

183. A solid support, wherein at least two oligonucleotides according to any of claims 176 to 178 are individually fixed to separate areas of the solid support to form an array.

184. The solid support according to claim 183, which is a glass chip, preferably a glass chip with a modified surface.

185. Use of the oligonucleotides of any of claims 176 to 179, or the kit of any of claims 180 to 182, or the solid support of claim 183 or 184, in a method according to any one of claims 122 to 136, 139 to 160, or 163 to 175.